PATENT COOPERATION TREATY

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From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

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NOTIFICATION OF TRANSMITTAL OF INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Rule 71.1)

Applicant's or agent's file reference 0122939	Date of Mailing (*day/month/year*) 11 OCT 2005
	IMPORTANT NOTIFICATION

International application No.	International filing date (*day/month/year*)	Priority date (*day/month/year*)
PCT/IL02/00174	05 March 2002 (05.03.2002)	05 March 2001 (05.03.2001)

Applicant

YISSUM RESEARCH DEVELOPMENT COMPANY OF THE HEBREW

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.

2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.

3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

4. **REMINDER**

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices)(Article 39(1))(see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

Name and mailing address of the IPEA/US Mail Stop PCT, Attn: IPEA/ US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (703) 305-3230	Authorized officer Stuart F. Baum Telephone No. 703-308-0196

Form PCT/IPEA/416 (July 1992)

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference Q122939	**FOR FURTHER ACTION**	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/IL02/00174	International filing date *(day/month/year)* 05 March 2002 (05.03.2002)	Priority date *(day/month/year)* 05 March 2001 (05.03.2001)
International Patent Classification (IPC) or national classification and IPC IPC(7): C12N 12/29, 15/82, 5/04. 15/29; A01H 5/00 and US CL: 536/23.1, 23.6, 24.1, 24.3; 435/ 468, 419; 800/278,		
Applicant YISSUM RESEARCH DEVELOPMENT COMPANY OF THE HEBREW		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 6 sheets, including this cover sheet.

   ☒ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 18 sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the report
   - II ☐ Priority
   - III ☒ Non-establishment of report with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
05 September 2002 (05.09.2002)	23 September 2005 (23.09.2005)
Name and mailing address of the IPEA/US Mail Stop PCT, Attn: IPEA/ US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (703) 305-3230	Authorized officer Stuart F. Baum Telephone No. 703-308-0196

Form PCT/IPEA/409 (cover sheet)(July 1998)

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/IL02/00174

I. Basis of the report

1. With regard to the elements of the international application:*

☐ the international application as originally filed.

☒ the description:
pages 1-80 as originally filed
pages NONE , filed with the demand
pages NONE , filed with the letter of .

☒ the claims:
pages NONE , as originally filed
pages NONE , as amended (together with any statement) under Article 19
pages NONE , filed with the demand
pages 81-98 , filed with the letter of 17 March 2005 (17.03.2005).

☒ the drawings:
pages 1-18 , as originally filed
pages NONE , filed with the demand
pages NONE , filed with the letter of .

☒ the sequence listing part of the description:
pages 1-45 , as originally filed
pages NONE , filed with the demand
pages NONE , filed with the letter of .

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.
These elements were available or furnished to this Authority in the following language _____ which is:

☐ the language of a translation furnished for the purposes of international search (under Rule23.1(b)).

☐ the language of publication of the international application (under Rule 48.3(b)).

☐ the language of the translation furnished for the purposes of international preliminary examination(under Rules 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

☒ contained in the international application in printed form.

☒ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☐ furnished subsequently to this Authority in computer readable form.

☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. ☒ The amendments have resulted in the cancellation of:

☒ the description, pages none

☒ the claims, Nos. 105-113

☒ the drawings, sheets/~~fig~~ none

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**

* *Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).*
** *Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.*

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The question whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been and will not be examined in respect of:

☐ the entire international application,

☒ claims Nos. 1-45 (in part) and 46-104

because:

☐ the said international application, or the said claim Nos. _____ relate to the following subject matter which does not require international preliminary examination *(specify)*:

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. _____ are so unclear that no meaningful opinion could be formed *(specify)*:

☐ the claims, or said claims Nos. _____ are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for said claims Nos. 1-45 (in part) and 46-104

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

☐ the written form has not been furnished or does not comply with the standard.

☐ the computer readable form has not been furnished or does not comply with the standard.

V. Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. STATEMENT

Novelty (N)	Claims 1-36	YES
	Claims none	NO
Inventive Step (IS)	Claims 1-36	YES
	Claims none	NO
Industrial Applicability (IA)	Claims 1-36	YES
	Claims NONE	NO

2. CITATIONS AND EXPLANATIONS

Claims 1-36 meet the criteria set out in PCT Article 33(2)-(3), because the prior art does not teach or fairly suggest an isolated nucleic acid comprising a polynucleotide encoding a boiling stable, detergent stable or protease resistant protein wherein said protein has chaperone-like activity, wherein the polynucleotide is operably linked to a promoter wherein the polynucleotide has a sequence at least 60% identical with SEQ ID NO:1, wherein said protein has a sequence at least 60% homologous to SEQ ID NO:2, or an isolated nucleic acid comprising a first polynucleotide encoding a boiling stable or detergent stable protein, wherein the protein has chaperone-like activity and wherein the first polynucleotide is adjacent to and in frame with a second polynucleotide encoding an additional protein, wherein the proteins encoded by the first and second polynucleotides form in combination a fusion protein, and wherein the first polynucleotide is operably linked to a third polynucleotide for directing an expression of said first encoded protein or fusion protein.

Claims 1-36 meet the criteria set out in PCT Article 33(4), and thus have industrial applicability because the subject matter claimed can be made or used in industry.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/IL02/00174

Supplemental Box
(To be used when the space in any of the preceding boxes is not sufficient)

Claims 1, 6, 9-13, 16, 21, 24-28, 31, 36, and 39-43, lack novelty under PCT Article 33(2) as being anticipated by Imanaka et al. The claims of the instant application are drawn to an isolated nucleic acid comprising a polynucleotide encoding a boiling stable protein, a detergent stable protein or a protease resistant protein, wherein said protein has chaperone-like activity and wherein the polynucleotide is operably linked to a promoter, wherein the promoter is a prokaryotic promoter, wherein the protein is natively an oligomer, wherein said chaperone-like activity includes heat stabilization of proteins, a nucleic acid construct comprising said polynucleotide, or a cell or organism transformed with said polynucleotide. Imanaka et al disclose a polynucleotide encoding a chaperon protein, GroESL, isolated from hyperthemophilic archaeon bacteria (page 5, line 9) subcloned into an expression cassette (pages 5-7), operably linked to a T7 promoter operable in prokaryotic bacteria (page 3, line 15) and transformation and expression in bacteria (page 7, example 3). Given Applicants definition of a boiling stable, detergent stable and protease resistant protein on page 30, lines 24-30 and page 31, lines 1-6 (i.e., "boiling stable" refers to major (above 50%) structural oligomeric stability following treatment at substantially 100C in aqueous solution for at least 10 minutes, "detergent stable" refers to major (above 50%) structural oligomeric stability of an oligomeric protein following treatment in aqueous solution containing 1/2000 molar ratio (monomer:SDS) and "protease resistant" refers to major (above 50%) stability following treatment in aqueous solution containing 50 ug per ml proteinase K for at least 60 minutes at 37C), respectively, it would be inherent that Imanaka's isolated polynucleotide would encode a boiling stable protein because it was isolated from an organism that lives at 80C or higher (page 5, lines 17-18) and said chaperone would also be detergent and protease resistant, and as such, Imanaka et al anticipate the claimed invention.

Claims 1-6, 9-13, 16-21, 24-28, 31-36, and 39-43 lack an inventive step under PCT Article 33(3) as being obvious over Imanaka et al. Given the teachings of Imanaka et al as discussed above, it would be obvious to substitute the prokaryotic promoter with a promoter operable in eukaryotic cells or organism, wherein the promoter is constitutive, or wherein the promoter is a constitutive and operable in plants, or wherein the promoter is selected from the list of promoters listed in claims 5, 20, or 35.

Claims 15, 30, and 45 lack an inventive step under PCT Article 33(3) as being obvious over Soto et al. The claims are drawn to a method of isolating a gene encoding a boiling stable, detergent stable or protease resistant protein having chaperone-like activity comprising screening an expression library with a polynucleotide encoding a boiling stable, detergent stable or protease resistant protein, respectively wherein said protein has chaperone-like activity. Soto et al teach isolating a small heat-shock protein that shows molecular chaperone activity. Soto et al teach isolating a cDNA that encodes said protein by screening a cDNA library with a nucleic acid encoding a sunflower HSP17.6. It would have been obvious to one skilled in the art to substitute the cDNA encoding the HSP17.6 with a cDNA encoding a boiling stable, detergent stable or protease resistant protein given the absence of evidence to the contrary.

Claims 7-8, 14, 22-23, 29, 37-38, and 44 meet the criteria set out in PCT Article 33(2)-(3), because the prior art does not teach or fairly suggest an isolated nucleic acid comprising a polynucleotide encoding a boiling stable, detergent stable or protease resistant protein wherein said protein has chaperone-like activity, wherein the polynucleotide is operably linked to a promoter wherein the polynucleotide has a sequence at least 60% identical with SEQ ID NO:1, wherein said protein has a sequence at least 60% homologous to SEQ ID NO:2, or wherein the polynucleotide encodes a fusion protein.

Supplemental Box
(To be used when the space in any of the preceding boxes is not sufficient)

Claims 1-45 meet the criteria set out in PCT Article 33(4), and thus have industrial applicability because the subject matter claimed can be made or used in industry.

WHAT IS CLAIMED IS:

1. An isolated nucleic acid comprising:

(a) a first polynucleotide encoding a boiling stable protein at least 60 % homologous to SEQ ID NO: 2, said boiling stable protein having a chaperone-like activity; and

(b) a second polynucleotide including a promoter sequence being operably linked to said first polynucleotide for directing an expression of said boiling stable protein.

2. The isolated nucleic acid of claim 1, wherein said promoter sequence is a eukaryote promoter.

3. The isolated nucleic acid of claim 2, wherein said eukaryote promoter is a constitutive promoter.

4. The isolated nucleic acid of claim 1, wherein said promoter is a plant promoter selected from the group consisting of a constitutive plant promoter, a tissue specific plant promoter and an inducible plant promoter.

5. The isolated nucleic acid of claim 4, wherein:

(i) said constitutive plant promoter is selected from the group consisting of CaMV35S plant promoter, CaMV19S plant promoter, FMV34S plant promoter, sugarcane bacilliform badnavirus plant promoter, CsVMV plant promoter, *Arabidopsis* ACT2/ACT8 actin plant promoter, *Arabidopsis* ubiquitin UBQ1 plant promoter, barley leaf thionin BTH6 plant promoter, and rice actin plant promoter;

(ii) said tissue specific plant promoter is selected from the group consisting of bean phaseolin storage protein plant promoter, DLEC plant promoter, PHSβ plant promoter, zein storage protein plant promoter, conglutin gamma plant promoter from soybean, AT2S1 gene plant promoter, ACT11 actin plant promoter

from *Arabidopsis*, napA plant promoter from *Brassica napus* and potato patatin gene plant promoter; and

(iii) said inducible plant promoter is selected from the group consisting of a light-inducible plant promoter derived from the pea rbcS gene, a plant promoter from the alfalfa rbcS gene, DRE, MYC and MYB plant promoters which are active in drought; INT, INPS, prxEa, Ha hsp17.7G4 and RD21 plant promoters active in high salinity and osmotic stress, and hsr203J and str246C plant promoters active in pathogenic stress.

6. The isolated nucleic acid of claim 1, wherein said promoter sequence is a prokaryote promoter.

7. The isolated nucleic acid of claim 1, wherein said stable protein is natively an oligomer.

8. The isolated nucleic acid of claim 1, wherein said chaperone-like activity includes heat stabilization of proteins.

9. A nucleic acid construct comprising the nucleic acid of claim 1

10. A cell transformed with the nucleic acid of claim 1.

11. An organism transformed with the nucleic acid of claim 1.

12. An isolated nucleic acid comprising:

(a) a first polynucleotide encoding a boiling stable protein, said boiling stable protein having a chaperone-like activity;

(b) a second polynucleotide including a promoter sequence being operably linked to said first polynucleotide for directing an expression of said boiling stable protein; and

(c) a third polynucleotide encoding an additional protein, said third polynucleotide being adjacent and in frame to said first polynucleotide, said first and third polynucleotides encoding, in combination, a fusion protein of said stable protein and said additional protein.

13. An isolated nucleic acid comprising:

(a) a first polynucleotide encoding a detergent stable protein at least 60 % homologous to SEQ ID NO: 2, said detergent stable protein having a chaperone-like activity; and

(b) a second polynucleotide including a promoter sequence being operably linked to said first polynucleotide for directing an expression of said detergent stable protein.

14. The isolated nucleic acid of claim 13, wherein said promoter sequence is a eukaryote promoter.

15. The isolated nucleic acid of claim 14, wherein said eukaryote promoter is a constitutive promoter.

16. The isolated nucleic acid of claim 13, wherein said promoter is a plant promoter selected from the group consisting of a constitutive plant promoter, a tissue specific plant promoter and an inducible plant promoter.

17. The isolated nucleic acid of claim 16, wherein:

(i) said constitutive plant promoter is selected from the group consisting of CaMV35S plant promoter, CaMV19S plant promoter, FMV34S plant promoter, sugarcane bacilliform badnavirus plant promoter, CsVMV plant promoter, *Arabidopsis* ACT2/ACT8 actin plant promoter, *Arabidopsis* ubiquitin UBQ1 plant promoter, barley leaf thionin BTH6 plant promoter, and rice actin plant promoter;

(ii) said tissue specific plant promoter is selected from the group consisting of bean phaseolin storage protein plant promoter, DLEC plant promoter,

(i) said constitutive plant promoter is selected from the group consisting of CaMV35S plant promoter, CaMV19S plant promoter, FMV34S plant promoter, sugarcane bacilliform badnavirus plant promoter, CsVMV plant promoter, *Arabidopsis* ACT2/ACT8 actin plant promoter, *Arabidopsis* ubiquitin UBQ1 plant promoter, barley leaf thionin BTH6 plant promoter, and rice actin plant promoter;

(ii) said tissue specific plant promoter is selected from the group consisting of bean phaseolin storage protein plant promoter, DLEC plant promoter, PHSβ plant promoter, zein storage protein plant promoter, conglutin gamma plant promoter from soybean, AT2S1 gene plant promoter, ACT11 actin plant promoter from *Arabidopsis*, napA plant promoter from *Brassica napus* and potato patatin gene plant promoter; and

(iii) said inducible plant promoter is selected from the group consisting of a light-inducible plant promoter derived from the pea rbcS gene, a plant promoter from the alfalfa rbcS gene, DRE, MYC and MYB plant promoters which are active in drought; INT, INPS, prxEa, Ha hsp17.7G4 and RD21 plant promoters active in high salinity and osmotic stress, and hsr203J and str246C plant promoters active in pathogenic stress.

18. The isolated nucleic acid of claim 13, wherein said promoter sequence is a prokaryote promoter.

22.Canceled

23.Canceled

19. The isolated nucleic acid of claim 13, wherein said stable protein is natively an oligomer.

20. The isolated nucleic acid of claim 13, wherein said chaperone-like activity includes heat stabilization of proteins.

21. A nucleic acid construct comprising the isolated nucleic acid of claim 13.

22. A cell transformed with the isolated nucleic acid of claim 13.

23. An organism transformed with the isolated nucleic acid of claim 13.

24. An isolated nucleic acid comprising:

(a) a first polynucleotide encoding a detergent stable protein, said detergent stable protein having a chaperone-like activity;

(b) a second polynucleotide including a promoter sequence being operably linked to said first polynucleotide for directing an expression of said detergent stable protein; and

(c) a third polynucleotide encoding an additional protein, said third polynucleotide being adjacent and in frame to said first polynucleotide, said first and third polynucleotides encoding, in combination, a fusion protein of said stable protein and said additional protein.

30.Canceled

25. An isolated nucleic acid comprising:

(a) a first polynucleotide encoding a protease resistant protein at least 60 % homologous to SEQ ID NO: 2, said protease resistant protein having a chaperone-like activity; and

(b) a second polynucleotide including a promoter sequence being operably linked to said first polynucleotide for directing an expression of said protease resistant protein.

26. The isolated nucleic acid of claim 25, wherein said promoter sequence is a eukaryote promoter.

Arabidopsis ACT2/ACT8 actin plant promoter, *Arabidopsis* ubiquitin UBQ1 plant promoter, barley leaf thionin BTH6 plant promoter, and rice actin plant promoter;

(ii) said tissue specific plant promoter is selected from the group consisting of bean phaseolin storage protein plant promoter, DLEC plant promoter, PHSβ plant promoter, zein storage protein plant promoter, conglutin gamma plant promoter from soybean, AT2S1 gene plant promoter, ACT11 actin plant promoter from *Arabidopsis*, napA plant promoter from *Brassica napus* and potato patatin gene plant promoter; and

(iii) said inducible plant promoter is selected from the group consisting of a light-inducible plant promoter derived from the pea rbcS gene, a plant promoter from the alfalfa rbcS gene, DRE, MYC and MYB plant promoters which are active in drought; INT, INPS, prxEa, Ha hsp17.7G4 and RD21 plant promoters active in high salinity and osmotic stress, and hsr203J and str246C plant promoters active in pathogenic stress.

30. The isolated nucleic acid of claim 25, wherein said promoter sequence is a prokaryote promoter.

31. The isolated nucleic acid of claim 25, wherein said resistant protein is natively an oligomer.

32. The isolated nucleic acid of claim 25, wherein said chaperone-like activity includes heat stabilization of proteins.

33. A nucleic acid construct comprising the isolated nucleic acid of claim 25.

34. A cell transformed with the isolated nucleic acid of claim 25.

35. An organism transformed with the isolated nucleic acid of claim 25.

PCT/IL02/00174 17032005
PEA/US 17 MAR 2005

36. An isolated nucleic acid comprising:

(a) a first polynucleotide encoding a protease resistant protein, said detergent stable protein having a chaperone-like activity;

(b) a second polynucleotide including a promoter sequence being operably linked to said first polynucleotide for directing an expression of said protease resistant protein; and

(c) a third polynucleotide encoding an additional protein, said third polynucleotide being adjacent and in frame to said first polynucleotide, said first and third polynucleotides encoding, in combination, a fusion protein of said resistant protein and said additional protein.

37. An isolated boiling stable polypeptide having a chaperone-like activity.

38. The polypeptide of claim 37, encoded by a polynucleotide having a sequence at least 60 % identical with SEQ ID NOs:1, 5, 6, 34, 39 or 40, as determined using the BestFit software of the Wisconsin sequence analysis package, utilizing the Smith and Waterman algorithm, where gap weight equals 50, length weight equals 3, average match equals 10 and average mismatch equals -9.

39. The polypeptide of claim 37, having a sequence at least 60 % homologous to SEQ ID NOs:2 or 35, as determined using the BestFit software of the Wisconsin sequence analysis package, utilizing the Smith and Waterman algorithm, where gap creation penalty equals 8 and gap extension penalty equals 2.

40. The polypeptide of claim 37 which is natively an oligomer.

41. The polypeptide of claim 37, wherein said chaperone-like activity includes heat stabilization of proteins.

42. An antibody recognizing at least one epitope of the polypeptide of claim 37.

43. A method of isolating a gene encoding a boiling stable protein comprising screening an expression library with the antibody of claim 42.

44. A method of preventing an aggregating protein from aggregating into an aggregate comprising causing an effective amount of the polypeptide of claim 37 to become in contact with said aggregating protein.

45. A method of de-aggregating aggregates of an aggregating protein comprising causing an effective amount of the polypeptide of claim 37 to become in contact with said aggregate.

46. A method of stabilizing a protein against denaturing conditions comprising causing an effective amount of the polypeptide of claim 37 to become in contact with said protein.

47. An isolated detergent stable polypeptide having a chaperone-like activity.

48. The polypeptide of claim 47 encoded by a polynucleotide having a sequence at least 60 % identical with SEQ ID NOs:1, 5, 6, 34, 39 or 40, as determined using the BestFit software of the Wisconsin sequence analysis package, utilizing the Smith and Waterman algorithm, where gap weight equals 50, length weight equals 3, average match equals 10 and average mismatch equals -9.

49. The polypeptide of claim 47, having a sequence at least 60 % homologous to SEQ ID NOs:2 or 35, as determined using the BestFit software of the Wisconsin sequence analysis package, utilizing the Smith and Waterman algorithm, where gap creation penalty equals 8 and gap extension penalty equals 2.

50. The polypeptide of claim 47 which is natively an oligomer.

51. The polypeptide of claim 47, wherein said chaperone-like activity includes heat stabilization of proteins.

52. An antibody recognizing at least one epitope of the polypeptide of claim 47.

53. A method of isolating a gene encoding a detergent stable protein comprising screening an expression library with the antibody of claim 52.

54. A method of preventing an aggregating protein from aggregating into an aggregate comprising causing an effective amount of the polypeptide of claim 47 to become in contact with said aggregating protein.

55. A method of de-aggregating aggregates of an aggregating protein comprising causing an effective amount of the polypeptide of claim 47 to become in contact with said aggregate.

56. A method of stabilizing a protein against denaturing conditions comprising causing an effective amount of the polypeptide of claim 47 to become in contact with said protein.

57. An isolated protease resistant polypeptide having a chaperone-like activity.

58. The polypeptide of claim 57 encoded by a polynucleotide having a sequence at least 60 % identical with SEQ ID NOs:1, 5, 6, 34, 39 or 40, as determined using the BestFit software of the Wisconsin sequence analysis package,

utilizing the Smith and Waterman algorithm, where gap weight equals 50, length weight equals 3, average match equals 10 and average mismatch equals -9.

59. The polypeptide of claim 57, having a sequence at least 60 % homologous to SEQ ID NOs:2 or 35, as determined using the BestFit software of the Wisconsin sequence analysis package, utilizing the Smith and Waterman algorithm, where gap creation penalty equals 8 and gap extension penalty equals 2.

60. The polypeptide of claim 57 which is natively an oligomer.

61. The polypeptide of claim 57, wherein said chaperone-like activity includes heat stabilization of proteins.

62. An antibody recognizing at least one epitope of the polypeptide of claim 57.

63. A method of isolating a gene encoding a detergent stable protein comprising screening an expression library with the antibody of claim 62.

64. A method of preventing an aggregating protein from aggregating into an aggregate comprising causing an effective amount of the polypeptide of claim 57 to become in contact with said aggregating protein.

65. A method of de-aggregating aggregates of an aggregating protein comprising causing an effective amount of the polypeptide of claim 57 to become in contact with said aggregate.

66. A method of stabilizing a protein against denaturing conditions comprising causing an effective amount of the polypeptide of claim 57 to become in contact with said protein.

67. A method of enriching or isolating a denaturant stable and/or protease resistant protein having chaperone-like activity from a biological source, the method comprising:

(a) extracting total proteins from the biological source so as to obtain a proteins extract;

(b) boiling said proteins extract;

(c) collecting soluble proteins; and optionally

(d) assaying for chaperone-like activity of the soluble proteins and enriching or isolating the stable protein having chaperone-like activity.

68. The method of claim 67, further comprising size fractionating said soluble proteins.

69. A method of isolating a gene encoding a denaturant stable and/or protease resistant protein having chaperone-like activity from a biological source, the method comprising:

(a) extracting total proteins from the biological source, so as to obtain a proteins extract;

(b) boiling said proteins extract;

(c) collecting soluble proteins;

(d) assaying for chaperone-like activity of the soluble proteins and isolating a stable protein having chaperone-like activity;

(e) raising antibodies recognizing said stable protein having said chaperone-like activity; and

(f) screening an expression library with said antibodies.

70. A method of isolating a gene encoding a denaturant stable and/or protease resistant protein having chaperone-like activity from a biological source, the method comprising:

(a) extracting total proteins from the biological source, so as to obtain a proteins extract;

(b) boiling said proteins extract;

(c) collecting soluble proteins;

(d) assaying for chaperone-like activity of the soluble proteins and enriching or isolating a stable protein having chaperone-like activity;

(f) microsequencing said stable protein so as to obtain at least a partial amino acid sequence thereof;

(g) designing an oligonucleotide corresponding to said amino acid sequence; and

(h) screening a library with said oligonucleotide.

71. A method of isolating a nucleic acid potentially encoding a denaturant stable and/or protease resistant protein having chaperone-like activity, the method comprising screening a cDNA or genomic library with a polynucleotide of at least 17 bases at least 60 % identical to a contiguous portion of SEQ ID NOs:1, 5, 6, 34, 39 or 40.

72. A method of identifying a nucleic acid potentially encoding a denaturant stable and/or protease resistant protein having chaperone-like activity, the method comprising searching an electronic library containing a plurality of nucleic acid and/or amino acid sequences for sequences having a predetermined degree of identity or homology to any of SEQ ID NOs:1, 2, 5-35 or 39-40 or portions thereof of, or corresponding to, at least 15 bases.

73. A method of isolating a nucleic acid potentially encoding a denaturant stable and/or protease resistant protein having chaperone-like activity, the method comprising:

(a) providing at least one pair of oligonucleotides each being at least 15 bases in length, said at least one pair of oligonucleotides including at least one oligonucleotide corresponding to SEQ ID NOs:1, 2, 5-35 or 39-40, said at least one pair of oligonucleotides being selected for amplifying a nucleic acid having a degree

of identity with, or encoding proteins homologous, to SEQ ID NOs:1, 2, 5-35 or 39-40;

(b) contacting said at least one pair of oligonucleotides with a sample of nucleic acid and amplifying said nucleic acid having said degree of identity with, or encoding proteins homologous to, SEQ ID NOs:1, 2, 5-35 or 39-40; and

(c) using said nucleic acid having said degree of identity with or encoding proteins homologous to SEQ ID NOs:1, 2, 5-35 or 39-40 for isolating a nucleic acid potentially encoding a denaturant stable and/or protease resistant protein.

74. A method of detergent-free isolation of a protease-resistant protein having chaperone-like activity from a biological source, the method comprising:

(a) extracting total proteins from the biological source, so as to obtain a proteins extract;

(b) contacting said protein extract with a protease; and

(c) isolating a protease-resistant protein; and optionally

(d) assaying said protease-resistant protein for chaperone-like activity.

75. A fusion protein comprising a denaturant stable and/or protease resistant polypeptide having a chaperone-like activity fused to an additional polypeptide.

76. The fusion protein of claim 75, wherein said denaturant stable and/or protease resistant polypeptide having said chaperone-like activity is fused to said additional polypeptide via a peptide bond.

77. The fusion protein of claim 75, wherein said denaturant stable and/or protease resistant polypeptide having said chaperone-like activity is fused to said additional polypeptide via a cross-linker.

78. The fusion protein of claim 75, having an oligomeric form.

79. A method of immunization comprising subjecting an immune system of a mammal to the fusion protein of claim 75.

80. A method of protecting an enzyme preparation from reduction in enzymatic activity, the method comprising adding to the enzyme preparation a denaturant stable and/or protease resistant protein, said denaturant stable and/or protease resistant protein having a chaperone-like activity, in an amount sufficient for protecting the enzyme preparation from reduction in enzymatic activity.

81. A method of repairing at least a portion of lost enzymatic activity of an enzyme preparation, the method comprising adding to the enzyme preparation a denaturant stable and/or protease resistant protein, said denaturant stable and/or protease resistant protein having a chaperone-like activity, in an amount sufficient for repairing at least said portion of said lost enzymatic activity of the enzyme preparation.

82. A method of administering to an animal having an immune system a polypeptide, while reducing an immune response against said polypeptide, the method comprising administering the polypeptide to the animal, said polypeptide being fused to a denaturant stable and/or protease resistant protein, said denaturant stable and/or protease resistant protein having a chaperone-like activity, thereby reducing said immune response against said polypeptide, as compared to an immune response that develops by administering to the animal the polypeptide alone.

83. A transgenic plant expressing a denaturant stable and/or protease resistant protein, said denaturant stable and/or protease resistant protein having a chaperone-like activity above a natural amount of said denaturant stable and/or protease resistant protein having said chaperone-like activity in said plant.

84. A method of rendering a plant more tolerant to a biotic or abiotic stress, the method comprising engineering the plant to express a denaturant stable

PCT/IL02/00174 17032005
IPEA/US 17 MAR 2005

and/or protease resistant protein, said denaturant stable and/or protease resistant protein having a chaperone-like activity, above a natural amount of said denaturant stable and/or protease resistant protein having said chaperone-like activity in said plant.

85. A method of rendering a plant more recoverable from a biotic or abiotic stress, the method comprising engineering the plant to express a denaturant stable and/or protease resistant protein, said denaturant stable and/or protease resistant protein having a chaperone-like activity, above a natural amount of said denaturant stable and/or protease resistant protein having said chaperone-like activity in said plant.

86. A method of increasing cell migration, the method comprising exposing said cells to an amount of a denaturant stable and/or protease resistant protein, said denaturant stable and/or protease resistant protein having a chaperone-like activity, sufficient for increasing cell migration.

87. A method of accelerating wound healing, the method comprising administering onto a wound an amount of a denaturant stable and/or protease resistant protein, said denaturant stable and/or protease resistant protein having a chaperone-like activity, sufficient for accelerating wound healing.

88. A method of inducing wound healing, the method comprising administering onto a wound an amount of a denaturant stable and/or protease resistant protein, said denaturant stable and/or protease resistant protein having a chaperone-like activity, sufficient for inducing wound healing.

89. A method of strengthening hair, nail or skin, the method comprising administering onto the hair, nail or skin an amount of a denaturant stable and/or protease resistant protein, said denaturant stable and/or protease resistant protein having a chaperone-like activity, sufficient for strengthening the hair, nail or skin.

90. A method of grooming hair, nail or skin, the method comprising administering onto the hair, nail or skin an amount of a denaturant stable and/or protease resistant protein, said denaturant stable and/or protease resistant protein having a chaperone-like activity, sufficient for grooming the hair, nail or skin.

91. A pharmaceutical composition, comprising, as an active ingredient, a denaturant stable and/or protease resistant protein, said denaturant stable and/or protease resistant protein having a chaperone-like activity, and a pharmaceutically acceptable carrier.

92. The pharmaceutical composition of claim 91, wherein said pharmaceutical composition is packaged in a package and identified in print for use in a wound healing application.

93. The pharmaceutical composition of claim 91, wherein said pharmaceutical composition is packaged in a package and identified in print for use in a strengthening and/or grooming hair, nail or skin application.

94. A method of isolating a boiling stable protein having chaperone-like activity from a biological source, the method comprising:

(a) extracting total proteins from the biological source, so as to obtain a proteins extract;

(b) boiling said protein extract;

(c) recovering soluble protein fraction; and optionally

(d) assaying said protease-resistant protein for chaperone-like activity.

95. The method of claim 94, further comprising digesting said protein extract with a protease.

PCT/IL03/00174 - 17032005
IPEA/US 17 MAR 2005

96. A method of treating a disease associated with protein aggregation of an aggregating protein, the method comprising administering to a subject in need thereof a denaturant stable and/or protease resistant protein, said denaturant stable and/or protease resistant protein having a chaperone-like activity, in an amount sufficient for de-aggregating and/or preventing aggregation of said aggregating protein.

97. The method of claim 96, wherein said aggregating protein is selected from the group consisting of beta-amyloid and prion.

98. A method of increasing a binding avidity of a binding molecule, the method comprising displaying multiple copies of the binding molecule on a surface of an oligomer of a denaturant stable and/or protease resistant protein, said denaturant stable and/or protease resistant protein having a chaperone-like activity.

99. The method of claim 98, wherein said binding molecule is selected from the group consisting of a receptor, a ligand, an enzyme, a substrate, an inhibitor, an antibody and an antigen.

100. A hetero complex comprising an oligomer including a plurality of a denaturant stable and/or protease resistant protein, said denaturant stable and/or protease resistant protein having a chaperone-like activity, and at least two different molecules being fused to said oligomer.

101. The hetero complex of claim 100, wherein said at least two different molecules comprise at least a first enzyme and a second enzyme.

102. The hetero complex of claim 100, wherein said first enzyme and said second enzyme catalyze sequential reactions in a synthesis or degradation pathway.

103. The hetero complex of claim 100, wherein said first enzyme and said second enzyme catalyze different reactions in a synthesis or degradation pathway.

104. The hetero complex of claim 101, wherein said at least two different molecules comprise at least a binding molecule and a reporter molecule.